Granuloma Inguinale

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GRANULOMA INGUINALE is generally considered a tropical disease, but the movement of masses of young men to and from the tropics during the war years may be expected to result in its extension to temperate climates. Even before the war it had spread all over the United States of America, from New York to San Francisco, and from Seattle to New Orleans, appearing first at the great seaports and spreading inland along the main lines of communication. No apology need therefore be made for writing on this subject, more particularly since two cases have been recognised in Belfast, in patients who have never left the United Kingdom, so that its presence here is a fact which must be faced by medical practitioners and considered when any intractable ulcerative condition of the ano-genital region is seen.

The writer has seen several hundred cases of the disease in the West Indies, and the following account of its clinical aspects is compiled from his experience.

The disease was first described by McLeod (1882) in Madras under the title of "Serpiginous Ulceration of the Genitals." Conyers and Daniels (1896), writing from British Guiana, gave a very detailed account of "The so-called lupoid ulceration of the genitals," and the histo-pathological changes were described by Galloway (1897) from material supplied by Conyers and Daniels. Donovan (1905) described intracellular inclusions in large mononuclear cells in cases seen in India, and these inclusions have since been termed Donovan Bodies (not to be mistaken for Leishman-Donovan bodies found in kala-azar). Later accounts were confused with different varieties of genital ulceration described under the title "granuloma inguinale," so that it is necessary to define the condition under discussion before proceeding further.

The three main ulcerative conditions found in the genital regions are chancroid and phagadenic ulceration, granuloma inguinale, and lymphogranuloma venereum. Chancroid and phagadenic ulcerations are too well known in temperate climates and do not require further description, but lymphogranuloma venereum and granuloma inguinale have been so confused that it is necessary to describe the disease condition referred to under each head.

Lymphogranuloma venereum affects primarily the lymphatic system of the genital region, with formation of inguinal buboes and subsequent ulceration which is rapidly progressive, destructive to the deeper tissues, with a foul-smelling purulent discharge, gives a positive Frei reaction, frequently causes rectal stricture, and the causative agent is a filter-passing virus. There may be variations in this picture. Buboes may appear and gradually fade away without ulceration, and in the female there may be no signs of the disease until rectal stricture develops as a result of localization of the infection in the lymphatic system of the pelvis, with subsequent fibrosis.

Granuloma inguinale on the other hand affects the skin and subcutaneous tissues

of the genital region with formation of a cellular granulation tissue, with subsequent fibrosis and scarring without obvious involvement of the lymphatic system, causes little or no pain or constitutional disturbance. It is a very chronic, slowly-progressive disease and in uncomplicated cases gives rise to a profuse non-purulent serous or sero-sanguineous discharge with a peculiar acrid odour. It does not ulcerate or invade the deeper tissues (except in cases complicated by secondary infection); the etiology is unknown, but it is associated with intracellular inclusions known as Donovan bodies.

It is unfortunate that two dissimilar conditions have been given such similar names; granuloma inguinale is referred to in the English literature as "lymphogranuloma inguinale," an unfortunate title, as it does not affect the lymphatic system. It has also been termed "ulcerating granuloma of the pudenda," another unfortunate title, as in uncomplicated cases it does not ulcerate; and granuloma venereum, which is better, except that it is liable to confusion with lymphogranuloma venereum.

A great deal of work has been done on these conditions by American observers in the last twenty or thirty years, and there the former condition is termed "lymphogranuloma venereum," and the latter "granuloma inguinale." It is proposed to use these two terms for the purpose of this paper to avoid confusion.

Granuloma inguinale is, as has been said, generally considered a tropical disease, but has recently been found in temperate zones, still more recently in our own country. Negroes are said to be more susceptible than other races, but it is doubtful if there is any real racial susceptibility. In my own experience in Trinidad, more cases were seen in persons of African descent, but as they form the largest racial unit in the island and comprise the great bulk of the most degraded section of the population, undernourished, sexually promiscuous, and living under the most insanitary conditions, morally and materially, they are thus more exposed to repeated opportunities of infection. Cases have been reported in all races—Negroes, Indians, Chinese, and Europeans. In England, all cases reported up to the present have been in persons such as seafaring people who have been exposed to infection in the tropics. The cases discovered in Belfast are both Europeon who have never been abroad and have had no contact with the tropics. They must, therefore, have acquired their infection locally, and are the first indigenous cases to be described in the United Kingdom.

Age Incidence.—The age incidence, as observed in Trinidad, is as follows:—

20 years and under	21 cases.
21 to 30 years	77 cases.
31 to 40 years	48 cases.
41 to 50 years	27 cases.
Over 50 years	15 cases.

Other observers give similar figures and it is apparent that the greatest incidence is at the age of greatest sexual activity.

Sex.—It is generally agreed that granuloma inguinale is more common in men than in women, and this is supported by the Trinidad figures. Of 188 cases observed at the Caribbean Medical Centre, 120 were male, and 68 female subjects.

Epidemiology.—Granuloma inguinale is generally considered a venereal disease contracted by sexual intercourse, but this is contested by some observers, as cases have been recorded in young children and accounts have been published of non-venereal cases. In endemic regions, however, it is always considered a venereal disease. No extra-genital cases have come under my observation.

Clinical.—The early lesion is a small raised patch of granulation tissue which is described as having started as a small papule or vesicle which bursts and spreads. This lesion is not an ulcer, it is raised above the level of the surrounding skin, the margin is sharply defined, firm, smooth and rolled, not punched out, ragged, or undercut. The surface is red, elevated, granular, and bleeds easily with a slight serous non-purulent discharge; there are no constitutional disturbances and the patient appears to be in ordinary health. The regional lymph nodes are not enlarged, the lesion is not painful, and there is little or no tenderness.

Early lesions are seen on the foreskin, glans, sulcus or shaft of the penis, and usually on the labiæ in the female.

Later lesions are an extension of the early lesion. They may develop by extension along the shaft of the penis or a fresh lesion may be found in the inguinal region. Some observers consider that the causative organism (said to be the Donovan body) spreads along the regional lymphatics, causing little disturbance on its way, localizes in the regional lymph nodes, and passes out to the adjacent skin to initiate the granulomatous process afresh in the inguinal region.

Later lesions are of a variety of types. They may be ulcerative, hypertrophic, or cicatricial. The so-called ulcerative (it is a bad term, as the condition is not an ulcer) type is an extension of the lesion just described and has the same characteristics—the raised granulomatous surface, an elevated, smooth, rolled but not undermined edge with a festooned outline, the surface bleeds easily, and is bathed in a plentiful sero-sanguineous non-purulent secretion with a peculiar acrid penetrating odour. It may be healing in one place, with formation of scar tissue, and progressing in another. Even in the presence of very extensive lesions the regional lymph nodes are not affected, there is no constitutional disturbance, no invasion of the deep tissues, or ulceration. It tends to spread along the moist surfaces in the scrotal folds, natal clefts, and anal region. Its progress is characteristically slow and chronic over a period of years, rather than months, if left untreated.

Although the skin of the ano-genital region is mainly affected, cases have been described in the mucus membrane of the vagina, urethra, and the cervix uteri, and of metastatic involvement of other organs, but the latter must be rare and was not seen in any of my Trinidad cases.

Late Lesions.—Complications due to secondary infection with various micro-organisms (fuso-spirochætosis, streptococci, and various ærobic and anærobic bacteria) are seen in a number of cases. The onset of such complications is indicated by constitutional symptoms, pain, purulent foul-smelling discharge, and an ulceration involving the deeper tissues. The granuloma is, however, as a rule, relatively insusceptible to secondary infection if the patient is reasonably clean and hygienic, but in the depressed classes of the population, who are undernourished, of insanitary habits, and addicted to excesses, such secondary infections are not uncommon.

Oedema and subsequent elephantiasis of the penis and scrotum in the male, and of the clitoris and labiæ in the female, are common.

Carcinoma of the genitals has occurred in a number of my cases, several of which showed on biopsy the histological structure of granuloma inguinale in one part and carcinoma in another.

Diagnosis.—The clinical features in the uncomplicated case are characteristic, and indeed diagnostic. The raised, non-purulent, granulomatous lesion with little pain or tenderness, showing no glandular involvement or constitutional symptoms, developing slowly, is a clinical picture not seen in any of the other venereal ulcerative conditions. Biopsy should be conclusive. The histological picture is characteristic, but might be mistaken by an observer not acquainted with granuloma inguinale for a malignant or pre-cancerous change. Donovan bodies are conclusive, but many intracellular bodies have been described in the literature wrongly as Donovan bodies. The superficial epithelial cells contain many inclusions, including bacteria, and can easily be mistaken for true Donovan bodies. For this reason, smears from the granulomatous area are unsatisfactory for diagnostic purposes. Moreover, the Donovan body is not easy to identify unless the observer is well acquainted with it and has good optical equipment. Confirmation of the diagnosis is therefore best obtained by biopsy.

Granuloma inguinale has not infrequently been mistaken for carcinoma, and the clinician should be on his guard when a lesion resembling carcinoma is seen in the genital region in young subjects.

Laboratory tests are of little or no value. There is no positive laboratory test for the presence of granuloma inguinale and positive serological tests, Frei, or Ducrey tests do not exclude it. All three were found positive with remarkable frequency in the Trinidad cases.

Treatment.—Intravenous injections of one of the preparations of antimony are specific in the early stages, but in old-standing cases cure may be difficult or even impossible. Surgery is required for removal of polpoid growths or elephantoid changes; X-rays and surgery for carcinomatous changes; secondary infection requires treatment with sulphonamides and penicillin. Surgical cleanliness, rest, good food, tonics, and general care of the health are all required.

Recently treatment with streptomycin is said to have had good effects in old intractable cases.

Specific Treatment.—Antimony was first employed by Aragao and Vianna in Brazil. They used one per cent. solution of tartar emetic in distilled water, 2 c.c. being injected every alternate day, slowly increasing the quantity until 10 c.c. was reached, then stopping all treatment for a week or two before commencing another course. Many such courses may have to be given and they should be continued for two or three months after healing is complete. Toxic symptoms such as dizziness, nausea, bone and joint pains, or diarrhœa are indications to stop treatment, but after a week or two it may be re-commenced with smaller doses.

The trivalent compounds of antimony are less toxic than tartar emetic. If a patient does not improve under treatment with one of the antimony preparations, another should be tried.

Prognosis.—This is a slow, chronic, progressive disease requiring great patience and continuous treatment. In the early stages antimony is specific, but, nevertheless, relapse is the rule even after complete healing and scarring has taken place. The patient must be kept under observation for years. Some cases progress in spite of all treatment and eventually develop constitutional symptoms, become cachectic, and die, but the disease may persist for twenty years or more, and the patient die of intercurrent disease.

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REVIEW

AIDS TO ANÆSTHESIA. By Victor Goldman, L.R.C.P., M.R.C.S., D.A. (R.C.P.&S.). Second Edition. Pp. viii + 316, with 85 illustrations. London: Baillière, Tindall & Cox. 1948. 7s. 6d.

THE first edition of this work in 1941 was eagerly welcomed, as it was an aid to all would-be anæsthetists. Now, in its new form, expanded and carefully revised, it has been brought up to date. Although he emphasises the fact that it is only an "Aid," the author has re-written a considerable part, and has made it more valuable as a book of reference.

From the preface, with its apt quotation, "No anæsthetic agent is safer than the person who employs it," to the valuable appendix of useful information, it is a book easy to read, as it is clear, concise, and clever. Who but the author would have likened the red blood corpuscles to barges on the canals of the transport system of the body?

The importance of teaching students how to use the open method is stressed. How often is a houseman able to give gas, oxygen, and ether, and yet would wonder which way to place a Schimmelbusch's mask?

Paradoxical respiration is clearly explained, and such modern drugs as trilene and curare dealt with. As regards prevention of post-operative pulmonary complications, the "hourly stir-up" is recommended—cruel to be kind. The diagrams and description of the Coxeter-Mushin absorber, which is terrifying at first sight to all students, the use of the Macintosh-Pask apparatus, so valuable in long intravenous anæsthetics, the description of the best method for a gastrectomy—the fashionable operation of the moment—are some of the new features, and are excellently presented.

The chapter on "Analgesia and Anæsthesia in Midwifery," by Dr. K. G. Lloyd Williams, has been modernised, and that on "Nitrous Oxide-Air Anæsthesia for Dentistry," by Dr. M. Hudson, has been revised and brought into line with the latest methods, although the mascara-laden tears of the first edition have disappeared.

Anæsthetists of all grades will welcome this work, and much can be learnt from it and from its excellent illustrations. It can be especially recommended to all who are teaching this subject to students and nurses. A larger, more complete textbook by the author, in his incomparable style, would be a welcome addition to modern medical works. V. L.